# Registries for Idiopathic Pulmonary Fibrosis: When Is It Time to Go Global?

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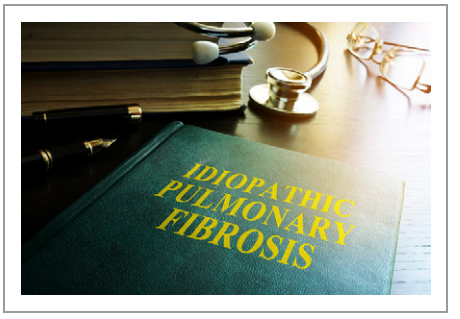
Registries have enhanced our knowledge of a variety of diseases, including idiopathic pulmonary fibrosis (IPF). In their article "Antifibrotic Drug Use in Patients with IPF: Data from the IPF-PRO Registry" in this issue of *AnnalsATS*, Salisbury and colleagues (pp. 1413–1423) investigated patterns of use of antifibrotic medications in the United States (1). The authors found that the majority of patients in the IPF-PRO (IPF Prospective Outcomes) Registry were receiving an approved medication for IPF at enrollment. Treatment at enrollment was associated with greater disease severity, more compromised quality of life, and the use of oxygen with exertion. The study confirms that physicians are more likely to prescribe antifibrotic drugs to patients with progressive IPF than to patients with milder forms (2).

Registries have an essential role in understanding disease and are particularly important in rare conditions. They facilitate the acquisition of new knowledge about prevalence, risk factors, and disease pathogenesis as well as patient management and treatment responses. They also allow more accurate real-life data collection than standardized clinical trials, which follow strict inclusion and exclusion criteria. Currently, patients included in clinical trials are often selected to maximize significant outcomes. In contrast, patients with IPF in registries often include those with more severe disease (3). Data from clinical trials are thus not necessarily applicable to real-life populations, especially when patients do not meet the same inclusion and exclusion criteria. Registries may also provide data when randomized clinical trials are not yet available. They could be used as a future platform for clinical studies that more closely represent real-world settings, albeit often showing less significant results for new drugs than trials do. This approach has not been tested for IPF yet.

Many IPF registries have been initiated and were described in a recent publication (3). Some registries collect data from patients with IPF from a single country, whereas others have been extended to several countries. These registries vary in the types of interstitial lung diseases that are included, and others focus specifically on individuals with IPF, with some already exceeding several thousands of patients (3). These registries complement data from clinical trials, and investigators are already using them to discover new biological aspects and validate preliminary results from smaller cohorts. Although existing disease registries are important, building and maintaining registries over a longer period of time can be tremendously challenging. Differences in diagnostic approaches and methodology result in substantial variability in the included patients across registries. This is amplified by changes in diagnosis over time (4, 5), the stage at the time patients are enrolled, and missing data (3).

Clinical data in registries should be complemented by biorepositories and imaging archives. Open access to such data would allow accelerated research for all scientists (6). Access to human lung tissues through commercial entities or through the Lung Tissue Resource Consortium (U.S. National Heart, Lung, and Blood Institute–funded consortium) has demonstrated the feasibility of this approach (6). The prospective collection and storage of blood, cell, and lung samples with longitudinal clinical phenotyping generated from various sources in a biorepository and linked registry has been suggested (6). But the collection of samples and imaging also needs to be standardized to allow high-quality data collection for research in a larger cohort.




Large registries for rare diseases have previously proven to be very helpful. The European registry for cystic fibrosis included in the project EuroCareCF, which is funded by the Sixth Framework Program of the European Commission, has proven that a large international registry is feasible and useful but also faces considerable challenges (7, 8). An international registry for IPF has been proposed repeatedly for more than a decade (9), but successful implementation has been elusive.

An attractive alternative to building a new global registry might involve merging existing data from current IPF registries. However, merging data on national and international levels can be challenging because of differences in data sets resulting in technical incompatibility, legal issues, and stakeholder conflicts of interests. Registries can have a great variability in data collection depending on the research question or intent behind the registry's development. Other challenges include threats to data quality based on retrospective and prospective data acquisition; changes in diagnostic definition over time implicate different diagnostic criteria for registries set up at different time points and difficulties in merging



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various imaging data. Together, these issues hinder the creation of a global registry. Artificial intelligence has been suggested to be used to overcome problems of data incompatibility (10).

A call to unite efforts to form a global registry with structured, defined, and focused goals and a proposed plan were made in 2014 (11). The suggested implementation was planned for 5 years, but still these efforts have yet to result in a global registry. Another European initiative, endorsed by the European Respiratory Society, the so-called Ariane-IPF ERS Clinical Research Collaboration project, aims to establish a platform for existing and new registries to share data and conduct common studies (12). This project includes a metaregistry, allowing subgroup and propensity analysis, which require large datasets.

All these efforts are time-consuming and costly. Infrastructures and resources for rare and new disease registries should be put in place to facilitate timely and coordinated prospective data collection to improve patient care for IPF and other diseases. Funding needs to be available to conduct prospective high-quality registries on any scale. Public funding for registries is difficult to obtain for various reasons (e.g., the ultimate goal is not clearly enough defined or too many outcomes are considered). Therefore, many registries rely on industry sponsors. It would be most desirable to have federal or national funding support for registries with clear research questions. National and international societies would also be ideal partners to coordinate and support data collection for registries on a global scale. Coordinating efforts would reduce the burden of administrative, regulatory, and funding obstacles and would decrease the number of registries that fail over time or do not result in meaningful research output. Common efforts are required to achieve these goals.

A global registry would be helpful to gain rapid standardized information about new unexplored diseases, disease courses, and disease outcomes. Although some efforts in this direction have already been undertaken, there is still a long way to go. Important steps toward this goal have already been made, and the enthusiasm of leaders in the field and the continuous work of all in this direction will help to achieve the goal of a global IPF registry. ■

**Author disclosures** are available with the text of this article at www.atsjournals.org.

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